MEDICAL STAFF CONFERENCE

Amebic Liver Abscess and Hydatid Disease

These discussions are selected from the weekly staff conferences in the Department of Medicine, University of California, San Francisco. Taken from transcriptions, they are prepared by Drs. Martin J. Cline and Hibbard E. Williams, Associate Professors of Medicine, under the direction of Dr. Lloyd H. Smith, Jr., Professor of Medicine and Chairman of the Department of Medicine.

DR. ELLIS:* This was the first University of California Hospital admission for this 46-year-old British woman. She was born in Malaysia, lived most of her life in India, Pakistan, Indonesia and Malaysia, and came to the United States in 1963. While in Pakistan in 1954 she had several episodes of dysentery of undetermined cause and an episode of transient jaundice associated with right-upper-quadrant pain. The cause of the jaundice was not determined, and treatment consisted of two to three weeks of bed rest.

The patient then had had no symptoms until, about two weeks before the present admission to UC Hospital, malaise, anorexia, myalgia, headache, and nasal congestion developed. Penicillin and novahistine were administered without relief. The symptoms progressed to nausea, vomiting, shaking chills, fever spikes to 39.4°C (103°F), night sweats, scleral icterus, and dull, constant, right-upper-quadrant pain.

The patient thereupon was admitted to another hospital, about a week before she entered the hospital here. Radiographic study of the chest showed no abnormality. Laboratory test results included: hematocrit, 35 percent; leukocytes, 30,000 per cu mm with a shift to the left; alkaline phosphatase, 30 Bodansky units (normal, 0 to 4); serum glutamic pyruvic transaminase, 39 units; and total bilirubin of 2.6 mg per 100 ml (direct, 1.9 mg per 100 ml). Common duct exploration was carried out. The liver was enlarged to 6 cm below the right costal margin, but no masses were noted. The gall bladder was normal and the common duct patent. A T tube was placed. Biopsy of a specimen of the liver taken by needle revealed essentially normal tissue, and biopsy of an enlarged lymph node in the porta hepatis revealed only reactive hyperplasia. Fever continued postoperatively, and a course of cephalothin and kanamycin was ineffective. On the fourth postoperative day the patient had a hypotensive reaction, tachycardia, and hemodilution. A large amount of serosanguinous fluid was removed by peritoneal tap. Cultures of blood, bile, sputum, urine, and fluid from the peritoneal cavity showed no growth. A search for ova and parasites yielded only Trichuris trichiura in one stool specimen. Amebiasis was considered, and serum was sent to the National Communicable Disease Center in Atlanta for an indirect hemagglutination test. The patient was then transferred to the University of California Hospital in San Francisco.

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On admission here, approximately two weeks after onset of the illness, the patient was acutely ill and had pronounced jaundice. A pulse of 120, blood pressure of 100/80 mm of mercury and rectal temperature of 37.8°C were recorded. Palmar erythema was observed, and a few spider angiomata were present on the anterior chest. There was no lymphadenopathy. Examination of the chest revealed right basilar dullness and decreased breath sounds. No cardiac abnormality was noted. Abdominal examination showed a well healed incision and drain in place in the right-upper-quadrant with bile draining from it. The liver was palpable 8 cm below the right costal margin. The spleen was not palpable. Bowel sounds were decreased, and a stool specimen was positive for occult blood. A finer tremor was present and the patient was disoriented as to time and place.

Laboratory studies on admission included: hematocrit, 32 percent; hemoglobin, 11 grams per 100 ml; leukocytes, 39,600 per cu mm with 80 percent polymorphonuclear cells, 3 percent lymphocytes, 5 percent monocytes, and 1 percent eosinophils; nonprotein nitrogen, 56 mg per 100 ml; creatinine, 1.7 mg per 100 ml; bilirubin, 7.1 mg per 100 ml (direct, 5.2 mg per 100 ml); total proteins, 5.2 (albumin, 2.1); alkaline phosphatase, 592 international units per liter (normal, 25 to 80); serum glutamic oxaloacetic transaminase, 227 units; serum glutamic pyruvic transaminase, 164 units; lactic acid dehydrogenase, 1,024; amylase, 27. Arterial gases showed a pH of 7.48, oxygen partial pressure of 50 mm of mercury, and carbon dioxide partial pressure of 32 mm of mercury. The cerebrospinal fluid was within normal limits. Radiographic study of the chest showed an elevated right hemidiaphragm and a right pleural effusion. A T-tube cholangiogram showed a patent common duct with extravasation of contrast material into the abscess. Right thoracentesis yielded 650 ml of transudate which was negative on culture. Cytological examination showed reactive mesothelial cells. A radioactive liver scan demonstrated a 4 x 7-inch defect in the right dome of the liver consistent with hepatic abscess. A celiac arteriogram showed hepatic arteries and branches normal except for stretching and displacement in the area of the liver abscess.

Exploratory laparotomy on the second hospital day revealed a huge abscess of the liver involving approximately half of the right lobe. Contents of the lesion appeared grayish and hemorrhagic and were necrotic throughout. The abscess did not have a limiting membranous wall and no fragments of membrane were seen. The lesion was surgically opened and two subcostal Penrose drains were placed. Examination of a Gram-stained specimen and routine culture of material from the abscess were negative. No amebas were seen after direct smear or concentration. Microscopic examination of liver tissue showed extensive areas of ischemic necrosis and central venous congestion but no bacteria or amebas.

The results of the indirect hemagglutination test for amebiasis, received four days after admission, revealed a titer greater than 1:4096, indicative of active invasive amebic disease. The Casoni skin test for Echinococcus granulosus was negative for both immediate and delayed reactions on two occasions, but scolices of Echinococcus granulosus were demonstrated in one stool specimen. Echinococcus multilocularis skin test antigen produced a small immediate reaction, a 1.4 cm wheal, but the delayed reaction was negative. Trichuris trichiura ova were seen in two stool specimens, but amebas were not seen by the Tropical Disease Laboratory on repeated examinations of ten specimens by direct, concentrated, and stained specimen techniques.

The patient's hospital course was characterized initially by low-grade fever, the temperature eventually returning to normal. Tracheal intubation was necessary for a few days following operation because of profound hypoxia associated with a significant arteriovenous shunt. An arterial oxygen partial pressure of 120 mm of mercury was obtained with the patient breathing 100 percent oxygen. A chest tube was placed in the right pleural space for drainage of pneumothorax which developed following thoracentesis. Repeated blood cultures were negative. Cultures of material from biliary, subcostal and endotracheal drainage, and of urine yielded only a scant-to-moderate growth of Candida albicans or parakrusei.

Therapy consisted of ampicillin, chloroquine, emetine, and diiodohydroxyquin. A short course of kanamycin was administered for pneumonitis thought to result from a proteus organism. Electrocardiograms were within normal limits and remained so during and after emetine therapy. The patient lost approximately 16 kg of weight. A T-tube cholangiogram shortly before discharge continued to show extravasation of contrast material into the abscess cavity, but the common duct re-

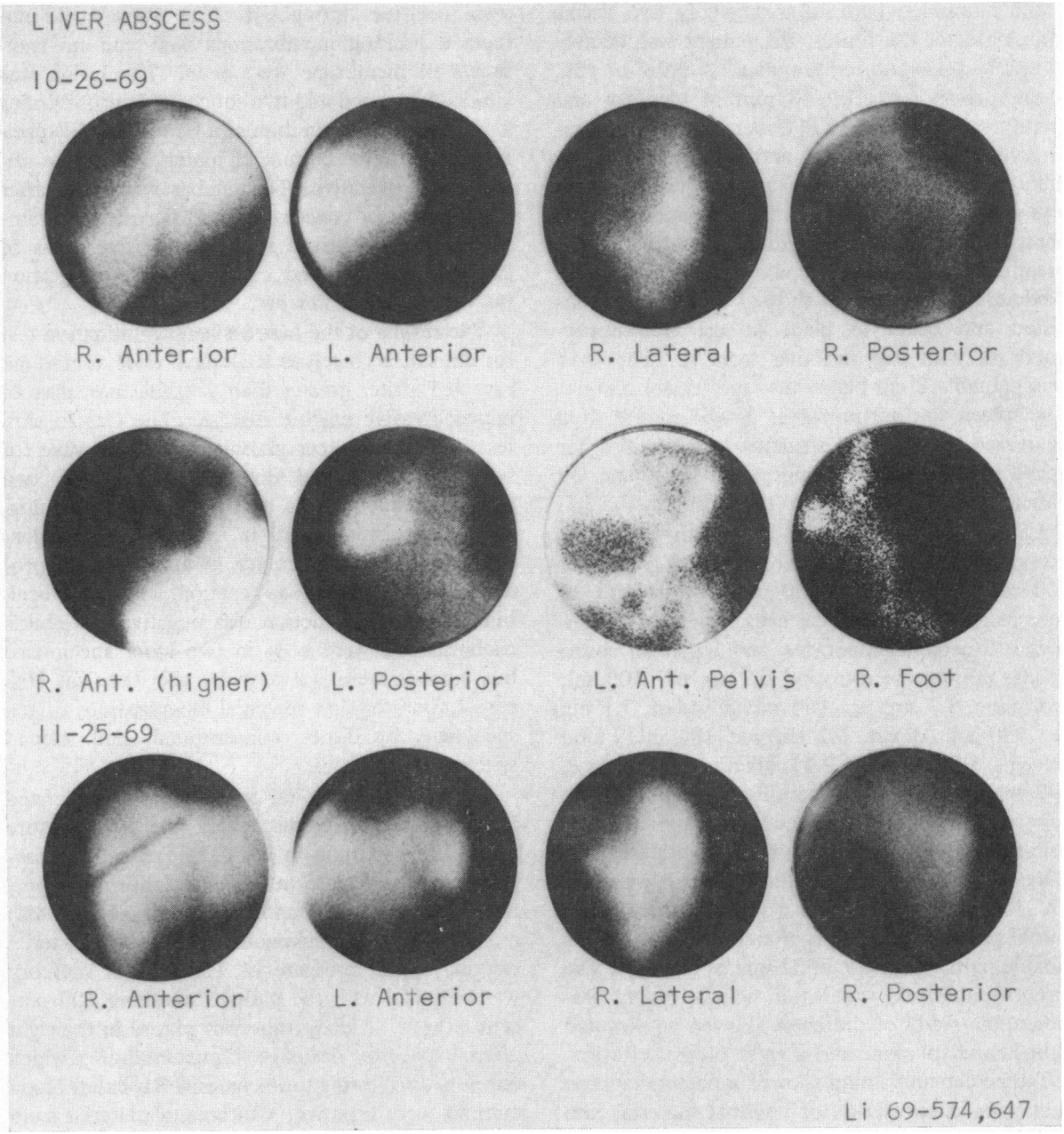

Figure 1.—Selected views from the liver scintiphoto study obtained during diagnostic evaluation October 26, 1969, and from a follow-up study November 25, 1969, are shown. The first study shows a giant defect laterally and posteriorly in the right lobe of the liver which can best be appreciated in the right anterior and right lateral view. Pronounced increase in bone marrow labeling and peripheral extension of bone marrow are also present. The follow-up study one month later demonstrates pronounced improvement with decrease of the giant defect of liver labeling within the liver substance.

mained patent. Although many values were normal, eosinophil levels of 9 and 10 percent were recorded on two occasions. At the time of discharge, one month after operation, the patient was ambulatory and afebrile. Leukocytes numbered 8,600 per cu mm and results of chemical studies referable to the liver had gradually returned to normal, except for continued elevation of the alkaline phosphatase.

DR. SMITH:* Thank you very much, Dr. Ellis. We are pleased to have Dr. Malcolm Powell to

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present the data on the radioactive liver scan in this patient.

DR. POWELL:* Two liver gammaphotographic studies were performed, with technetium sulfur colloid used to label the reticuloendothelial elements within the liver (Figure 1). The first study established the presence of a large space-occupying lesion within the liver which was consistent with the diagnosis of liver abscess. The second study was performed nearly a month later, after therapy for the abscess. The liver reticuloendothelial tissue was evenly distributed and the resulting gammaphotos were of extremely high spatial resolution.

The original gammaphotographic study showed a giant defect of labeling in the region of the right lobe of the liver above the level of the inferior costal margin. In the lateral view, the abscess occupied the entire posterior segment of the right lobe of the liver and displaced the liver quite far anteriorly. This anterior displacement caused the liver to appear as a very faint image in the posterior view, since it was farther away from the detector and there was less available radiation to form the image. The defect had slightly irregular but discrete margins. It was not a single spherical defect entirely within the liver, as is often seen with amebic abscess. In the right anterior view of the diaphragmatic area (second row of gammaphotos in Figure 1) faint images of rib marrow spaces were superimposed over the large negative defect associated with the abscess. Lung labeling was visible above the level of the defect. Small amounts of technetium colloid were localized in lungs owing to the presence of larger sized particles in the radiopharmaceutical preparation. An interesting defect was seen superiorly and laterally in the spleen image in the left posterior view. This was quite small, less than a half inch in diameter, and would be consistent with granulomatous disease, splenic infarct, or other small abnormality within the spleen. The image of the left foot showed the extreme peripheral extension of bone marrow sometimes seen in response to infection. The os calcis was particularly well labeled, but label was seen to extend out into the phalanges of the toes.

The second study, performed a month after initiation of therapy, showed a remarkable change in the liver outlines. The liver was a recognizable liver shape with considerable labeling of liver substance above the level of the costal margin, as indicated by a lead marker in the anterior view photo. The lead marker was not seen in the first study because it was superimposed over the unlabeled abscess. The liver lay very low, so that it was largely below the costal margin. The anterior view did not clearly define the previous defect, but a defect still was present in the right lateral and the posterior views. At this time, the liver was seen much better in the posterior view than it was before, because its position had shifted posteriorly with resolution of the abscess. It should be noted that there was some irregularity of liver labeling throughout, consistent with hepatocellular disease. No major focal abnormalities were seen except those residual from the previous abscess.

These studies gave excellent demonstration of the usefulness of liver gammaphoto studies in defining the presence of liver disease and its location within the liver substance so that specimens can be taken from the right sites for diagnosis by biopsy. Also illustrated was the value of routine imaging of the spleen and marrow when liver gammaphoto studies using ^{99m}technetium sulfur colloid are performed.

DR. SMITH: This desperately ill patient was seen by many members of the house staff as well as members of the faculty and various specialty groups during her prolonged stay here. We have asked Dr. Robert S. Goldsmith from the Hooper Foundation to open the discussion of her illness.

DR. GOLDSMITH:* The clinical diagnosis of liver abscess was not too difficult in this patient's case. Clinical findings preceding operation included fever, prostration, right upper-quadrant pain, and an enlarged and tender liver—all cardinal signs and symptoms of hepatic abscess. A liver scan showed the abscess to be in the right lobe. The diagnosis preoperatively was amebic abscess, pyogenic abscess, or a combined infection. At operation, however, the abscess did not have the characteristic features of either infection, and examination of its contents showed no bacteria or trophozoites.

Thus the specific diagnosis remained uncertain for several days after the operation. Because the patient was so ill, treatment was begun with both antibiotics and chloroquine so that pyogenic or-

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ganisms and amebas, if present, would be destroyed. On the fourth day after admission, two laboratory reports delivered within hours of each other confronted us with the suggestion of an interaction between an unexpected pair of etiologic agents: Entamoeba histolytica and Echinococcus granulosus. In reviewing the literature, I found no similar report in which amebiasis and hydatid disease appeared simultaneously in relation to a liver abscess.

The diagnosis of amebiasis in this patient's illness is based upon a high amebiasis antibody titer by the indirect hemagglutination test. The diagnosis of hydatid disease is based upon the remarkable parasitologic evidence of hydatid scolices in the stool. How did scolices get into the gastrointestinal tract, since scolices are usually enclosed completely within the walls of a hydatid cyst and hydatid cysts are generally contained within the liver? I surmise that a hydatid cyst in the patient's liver leaked or ruptured into the abscess cavity and some cyst contents later passed via the biliary system into the gut and hence into stool. We know from T-tube cholangiograms that the biliary radicles were in direct contact with the abscess cavity.

Whether the patient's abscess contained a pyogenic component in addition to the amebic infection is still not known. I am inclined to believe that this abscess, as in a small proportion of all liver abscesses,[1] was the result of a combined infection. The high leukocyte count (40,000 per cu mm), jaundice, and other liver function abnormalities are findings more characteristic of a pyogenic than of an amebic abscess, although all may occur in an amebic abscess alone.[2,3] Direct smears and subsequent cultures of the abscess contents were negative for bacteria, but pyogenic organisms are often absent in pus aspirated from the center of an abscess because of autolysis. Also, organisms may be absent in pus from the periphery of an abscess if a patient has been treated with antibiotics, as this patient had been for several weeks.

Source of Infection

We can only speculate on the sources of this patient's infections. She may have acquired the hydatid infection when she lived near Perth, Australia, in a rural sheep and cattle area during World War II. That was 25 years ago, but most hydatid cysts grow slowly (often for the lifetime of the patient) and require up to a decade to become large enough to manifest themselves by exerting pressure or by rupturing. No Taenia ova were found in the stool of the patient's present dog, but no purge was used to obtain the specimen. The patient could have acquired the amebic infection during her past seven years' residence in the United States, considering that the prevalence in different areas of this country in 1961 was estimated at 2 to 6 percent.[4] But it is far more likely that the amebic infection was acquired while she was living abroad, either in Malaysia, Indonesia, Pakistan, or India—countries where the disease is highly prevalent. It is not unusual for an asymptomatic amebic intestinal infection to persist for many years and ultimately give rise to an acute amebic abscess of the liver. In fact, 30 to 40 percent of patients with proven amebic abscesses of the liver give no history of dysentery. This patient had experienced sporadic episodes of mild-to-moderate diarrhea while abroad, but she had had no significant intestinal symptoms while living in this country.

Amebiasis

Diagnosis

In recent years serologic tests have been developed as aids in the diagnosis of amebiasis.[5] The indirect hemagglutination (IHA) test[6,7] is now available to physicians in the United States for clinical use. However, because no satisfactory commercial antigen has been marketed, local laboratories cannot perform this test. At present, therefore, we rely upon the Parasitology Section of the National Communicable Disease Center (NCDC) in Atlanta, Georgia, for this service. The serum should be separated under aseptic conditions and sent unfrozen by airmail. Specimens are processed promptly at NCDC and results can be obtained by telephone within one to two days after receipt.

A low positive titer (1:128 to 256) means either that the patient has an active infection or has had amebiasis and is cured. At these titers the antigen does not appear to cross-react with antibodies from any other disease. High titers (1:2,048 or greater) are more often associated with active disease. The IHA test cannot be used to distinguish between amebic infections of the liver and of the intestinal tract. A positive test result simply means infection in either or both sites.

When the test is used to detect amebic liver abscess, false negatives occur in less than 5 percent of patients. Because the test is so sensitive and specific for amebic abscess, it can be used with considerable confidence to confirm the diagnosis in the case we are discussing. Repeat titrations on two specimens of the patient's blood gave endpoint titrations of 1:32,700 and 1:131,000.

The IHA test is less sensitive in amebic infections of the intestinal tract. In amebic dysentery, a condition in which trophozoites invade the intestinal wall, false negative results may occur in up to 15 percent of proven cases. In asymptomatic intestinal infection the parasite is generally not invasive and false negatives have been reported in 35 to 90 percent of patients known to have an intestinal infection.

Additional parasitologic tests in suspected cases of amebic liver abscess should include examination of the intestinal tract and the abscess for amebas. Stools should be examined for trophozoites and cysts on at least six occasions. If immediate examination is not possible, the specimen should be placed in a preservative. Proctosigmoidoscopy should also be conducted to search for mucosal ulcers. If seen, ulcers should be scraped; the contents should be placed in a drop of saline and then promptly searched for trophozoites. At endoscopy a specimen of the ulcer should be taken for biopsy. If no ulcers are present, biopsy material should be taken from normal mucosa. Occasionally biopsy has been the sole means for establishing a morphological diagnosis. Nevertheless, intestinal amebas are found in only 15 percent of patients with amebic liver abscess who are free of bowel symptoms.

Amebic abscesses are often aspirated both for diagnostic and therapeutic purposes. For therapeutic reasons, aspiration need only be done on large abscesses to hasten the healing process and prevent rupture. Pus from amebic abscesses is classically described as "anchovy" in color, but it may range from creamy-white to chocolate, with specks of blood often seen. In the absence of secondary infection, the pus has a musty odor. Aspiration should be done by an experienced person, as there is a potential hazard in the introduction of bacteria followed by secondary infection. The procedure should be carried out under maximal aseptic conditions in the surgical amphitheater. Trophozoites are best found in aspirate from the edge of the cavity, not from the center where autolysis occurs. If very thick, the pus should be thinned before examination by incubation at 37°C for 30 minutes with streptokinase-streptodornase. If immediate examination cannot be carried out the aspirate should be fixed in polyvinyl alcohol. Amebic cultures should be requested if the laboratory procedure is available.

Other diagnostic tests for amebic liver abscess include the radiologic methods used to study this patient's illness. Eosinophilia is not commonly present. Most reports in the literature indicate that liver function abnormalities are inconsistent and contribute little to the diagnosis.[2,3,8] The most common changes are retention of bromsulphalein, elevation of alkaline phosphatase and serum globulin, and reduction of albumin. Jaundice is unusual and when present suggests a very large abscess obstructing the biliary system. In the present case, alkaline phosphatase was elevated to four times the normal level two weeks after operation, at a time when the bilirubin and other liver function tests were returning to normal. Although the alkaline phosphatase level may fall slowly, we were perplexed by its failure to decrease in this case. Elevations have been reported in cases of rupture of hydatid cysts into the biliary tract.[9] Several other potential causes in addition to the abscess could not be implicated: The common duct was patent and, although the patient had received a large amount of serum albumin over a two-week period, none of it, to our knowledge, was of placental rather than venous origin. Serum albumin from placental sources would be expected to sustain an alkaline phosphatase elevation.*[10]

Treatment[5,11,12]

Treatment of the abscess in the present case consisted of surgical drainage, antibiotics, and specific anti-amebic therapy with chloroquine and emetine. Diiodohydroxyquin (Diodoquin®) was given to eradicate amebas, if present, from the gastrointestinal tract. The combination of chloroquine and emetine is currently the treatment of choice for amebic liver abscess. Relapses are more commonly seen when either drug is used alone than when they are used together.[3] Because the patient was very debilitated, she was given 30 mg of emetine daily for ten days, half the usual dosage, but she received a standard dosage of chloroquine, 250 mg twice daily for four weeks.

*Six weeks after discharge the patient's alkaline phosphatase level had returned to normal.

The new synthetic drug dehydroemetine[11] may replace emetine. In experimental animals dehydroemetine is less toxic and is excreted more rapidly than emetine, but until additional clinical experience is obtained, the same cautions and contraindications should be followed for dehydroemetine as for emetine. In the United States, dehydroemetine is not yet approved for clinical use but may be obtained for use on an investigational basis from the NCDC.*

Hydatid Disease

The etiologic agent in hydatid disease (echinococcosis) is usually Echinococcus granulosus. Echinococcus multilocularis is less often a causative organism and produces a different, more life-threatening disease characterized by a neoplastic-like invasive process. My comments will be limited to E. granulosus.

Hydatid disease resulting from E. granulosus is prevalent in many parts of the world and is hyperendemic in the great sheep and cattle raising regions. In most cases diagnosed in humans in the United States the infection occurred abroad. However, hydatid disease acquired in this country has been reported from most regions and specifically from 16 states. Infection is present in sheep in California, autochthonous human cases have also been reported, and recently the entire parasitic transmission cycle has been demonstrated on a Basque shepherd's farm in the Central Valley of this state.[13]

The Parasite

The adult form of the parasite, a tiny tapeworm 3 to 6 mm long, is found in the intestines of dogs, wolves, and other members of the family Candidae. Ova are released from the terminal segment of the adult tapeworm and pass in the feces to the ground. Herbivores, particularly sheep, cattle, and hogs, ingest the ova while feeding. Man becomes infected only by inadvertently ingesting the ova. In both grazing animals and man the hexacanth embryo hatches from the ova, penetrates the intestinal wall, and is carried in the vascular channels to the liver and other organs and tissues where it develops into a hydatid cyst—the larval form of the parasite. The parasite's life cycle is completed when a carnivore ingests the viscera, particularly the liver, of the infected herbivore. Scolices within the cyst then mature into numerous adult tapeworms in the carnivore's intestine. The adult tapeworm cannot develop in man's intestine; therefore, man serves only as a "dead end," accidental, intermediate host for the parasite.

Pathogenesis in Man

Because the liver is the first organ to screen the flow of mesenteric blood, most hydatid cysts are found there. Some embryos pass through the liver, gaining access to other organs and tissues. The lung is the next most common site of infection and other sites less often infected include the spleen, heart, bones, and central nervous system.

When man is infected with E. granulosus, usually only one cyst develops in the liver. The characteristically unilocular cyst has a laminated wall whose thick outer portion, formed as a protective device by the host, is composed of dense, fibrous connective tissue. The thin inner portion, derived from the parasite, contains several structures, the most important being an innermost "germinal" layer. This layer gives rise to daughter colonies and to numerous individual scolices similar to those found in the stool of the patient in the present case. The host is protected from the capacity of the scolices to develop into new hydatids so long as the scolices remain within the cyst wall. Should the cyst wall break, however, scolices and daughter colonies (brood capsules) escape and may be seeded in nearby areas to form secondary cysts.

A hydatid cyst of the human liver grows slowly, reaching a diameter of 1 to 2 mm in two months. Most cysts attain a diameter of 1 to 7 cm, but larger ones containing several liters of fluid may occur. Patients are usually asymptomatic until a cyst becomes so large or is so situated as to cause pressure, or it ruptures or becomes infected.

Rupture is a frequent complication, since hydrostatic pressure within a cyst is several times greater than that of the surrounding liver tissue. The cyst may rupture, spontaneously or because of trauma, into the biliary system or into the abdominal or chest cavities. The three classical features of rupture into the biliary system are right upper-quadrant pain, jaundice, and allergic reactions.[9,14,15] Diagnosis of rupture is confirmed when scolices or portions of cyst wall or both are found in the stool.

Figures 2 and 3 are photographs of a scolex found in the patient's stool in the present case. The scolices recovered were typical of invaginated

*Dr. Myron Schultz, Parasitic Diseases Branch.

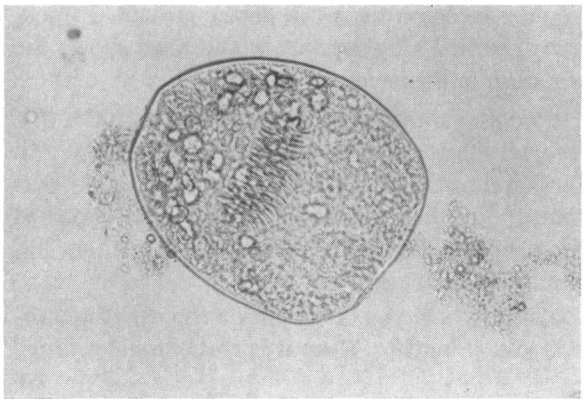

Figure 2.—Hydatid scolex found in the patient's stool.

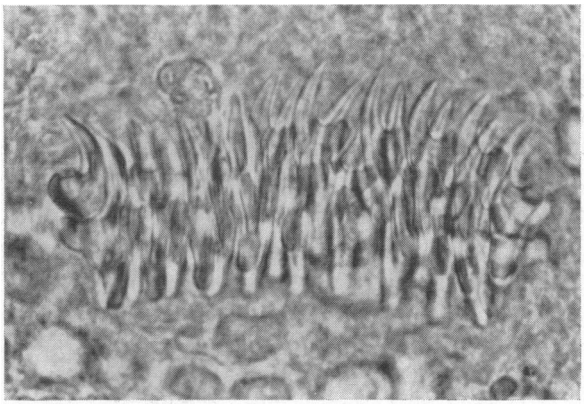

Figure 3.—Enlarged view of scolex showing hooklets.

Echinococcus scolices containing diffuse calcareous granules and a central cluster of taenia-like hooklets. The scolex illustrated measured 135 by 162 μ—within the expected range for E. granulosus. The hooklet count in the specimen was 28, about the minimum number usually found. Individual hooklets are approximately 30 μ long.

Diagnosis

A large and tender liver usually suggests the diagnosis of hydatid cyst in a patient who has resided in an endemic area. Clinical and laboratory findings that support the diagnosis include: eosinophilia (occurring in about 25 percent of patients), a "hydatid thrill" (occasionally seen in patients with very large cysts), calcification of the cyst wall (seen on flat x-ray films of the abdomen), and a space-occupying lesion in the liver (revealed by radioisotopic scan or other radiologic techniques).

Several immunologic tests also facilitate diagnosis. The Casoni intradermal skin test gives positive results in 70 to 95 percent of proven cases, but false positives have been reported in as many as 17 percent of controls.[16] The Casoni test is read at 15 minutes and at 18 to 24 hours and should be compared with a control saline solution injection. Two serologic tests are performed by NCDC, the IHA test (diagnostic titer, 1:400 to 800) and the bentonite flocculation (BF) test (diagnostic titer, 1:5). The IHA test gives positive results in approximately 83 percent of proven cases and false positives in the range of 1 to 3 percent.[16]

In the present case the history of repeated abdominal pain and jaundice ten years ago is compatible with recurrent leaking from a hydatid cyst, a syndrome described by other observers.[15] During the present illness eosinophilia was noted twice, but cyst wall calcification was not found on x-ray examination. The IHA and BF serologic tests were negative. Casoni skin tests using two different sources of E. granulosus antigen were negative when conducted immediately before and after operation. When I used an E. multilocularis antigen four weeks after operation, I obtained a reaction interpreted as borderline positive: At 15 minutes the maximum wheal diameter was 1.4 cm, the minimum diameter 1.0 cm, and the control 0.6 cm. At 18 hours no reaction was present. A negative immunologic response in the presence of a live hydatid cyst is unusual. Had this patient had a hydatid cyst in the lung, in the event of cyst rupture scolices could have been coughed up and then swallowed. Poor immunologic responsiveness would then be anticipated. However, an x-ray film of the chest at the onset of illness showed no abnormality. Radiographs of bones for extopic lesions should be done.

I cannot say precisely when, in the present case, the hydatid cyst in the liver ruptured into the abscess or biliary tract during this illness. It may have been at any time during the rapid extension of the amebic abscess or at the time of surgical evacuation. No remnants of cyst wall were seen at operation, nor were cyst elements found at pathologic examination of the abscess contents. Later, repeated examinations of material that drained from the abscess, the T tube and the right pleural space were also negative. The cyst may have been small, completely surrounded by the abscess, and after rupture its germinative elements destroyed by the necrotizing process. I do not know whether the pathologic process of an amebic abscess, usually a bacteriologically sterile colliqua-

tive necrosis, would destroy all elements of a hydatid cyst, including the outer wall. A pyogenic infection of a hydatid cyst would not. If the cyst is large and remains relatively intact, it should become visible on subsequent liver scans as the liver regenerates in the area of the amebic abscess.

Therapy of Hydatid Cysts[17]

Percutaneous aspiration of a hydatid cyst for diagnostic or therapeutic reasons is very dangerous and must not be done. No chemotherapeutic drugs are available, although a desensitization procedure with some claims to effectiveness has been reported from South America. Surgical removal or marsupialization is the only treatment if the cyst is accessible. Meticulous care must be exercised in removing hydatid fluid to avoid leakage which might lead to seeding of secondary cysts or hypersensitivity reactions, including anaphylactic shock. The cyst cavity is then filled with a scolicidal agent to sterilize the remaining contents before removal of the cyst wall.[18]

Prognosis

The prognosis for the patient in the present case with respect to the amebic infection is good. Nevertheless, she has approximately a 7 percent chance for recurrence of the amebic abscess, which would require a second course of treatment. One must be alert to the possibility that a pyogenic infection could recur as well. With respect to the hydatid infection, however, the prognosis is uncertain. A hydatid cyst has probably ruptured into the patient's biliary system with possible dissemination of germinative elements to other tissues. Some cures have been reported after such ruptures, but the disease is usually progressive and the prognosis poor.

DR. SMITH: Thank you, Dr. Goldsmith. I would like to ask Dr. John Conte to comment on the opinions of the infectious disease group.

DR. CONTE:* First, I would like to make a plea for the use of proctosigmoidoscopy and biopsy to demonstrate the etiologic agent. True, we had the serologic studies but we did not have an organism and we were confronted during treatment of this patient with the development of symptoms that suggested drug toxicity: increased alkaline phosphatase and development of eosinophilia. We would have been on much firmer ground, I think, if we had had a biopsy that would have shown the organism in the intestinal mucosa.

Second, I would like to ask Dr. Goldsmith if it would not have been of value to begin therapy with Diodoquin earlier. Was there any reason to wait before directing treatment toward the intestinal phase of this disease? Presumably the patient has intestinal amebiasis.

Third, would you comment on the use of metronidazole (Flagyl®), since it is so nontoxic a drug?

DR. GOLDSMITH: I agree that proctosigmoidoscopy should be employed as early as possible in such patients to aid in obtaining a morphologic diagnosis. This patient's condition was so critical after operation that the procedure could not be used. It should have been tried later. However, since treatment with emetine rapidly destroys trophozoites and promotes healing of mucosal ulcers, organisms would not have been found some days after use of the drug was begun.

Concerning your second question, about the use of Diodoquin: Neither emetine nor chloroquine is effective against organisms in the intestinal lumen, although emetine acts against organisms in the intestinal wall. Therefore, a luminal amebicide such as Diodoquin must be given to every patient treated for hepatic amebiasis. It is possible that the patient in the present case no longer had an amebic infection of the gastrointestinal tract when she was admitted to hospital. On the other hand, our inability to find amebas or cysts in the stools does not rule out their presence. As to the proper time to begin Diodoquin treatment, I thought it preferable to begin its use midway in the patient's course of chloroquine and emetine to reduce the number of drugs she was taking the week after operation.

The question about the use of Flagyl is anticipated. Reports now coming in from various parts of the world indicate that it is extremely effective for the treatment of amebiasis. It is the drug of choice for the systemic treatment of trichomoniasis. Side effects at standard doses are minor, but when the drug is used for amebic liver abscess or intestinal disease it must be administered at three times the normal dosage given for trichomoniasis. We therefore need additional clinical experience to be sure that significant side effects do not accompany higher doses of Flagyl. I was concerned about using an investigational drug for a patient

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whose clinical condition was so critical. In addition, Flagyl is not yet approved for treatment of amebiasis in the United States. I expect, however, that it will be approved and become the drug of choice for both extraintestinal and intestinal amebiasis. An important feature of Flagyl is its simultaneous effectiveness against both the intestinal and liver phases of amebiasis. Another new drug, niridazole (Ambilhar®), also has this property, but it has more side effects than Flagyl.

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DEAF-BLIND CENTER SYSTEM PROJECT

The Southwest Regional Center for Deaf-Blind Children has been established in Sacramento, serving the geographic area of California, Arizona, Nevada and Hawaii. The program is funded through the Elementary and Secondary Education Act, Title VI-C.

The primary objective of the Center is to locate and identify deaf-blind children in these areas and concurrently to provide and make available comprehensive diagnostic and educational services for these children. Consultative services will also be provided to those directly involved with the deaf-blind child.

Dr. William A. Blea is the project director for the four-state region. For either reporting of identified deaf-blind children or information regarding services contact Dr. Blea at:

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